

Neuronal identity and maturation

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Statements

belonging to the PhD thesis

Neuronal Identity and Maturation

Insights from the Single-Cell Transcriptome

Mark van den Hurk, 13 december 2016

1. DMEM/F12- or Neurobasal-based neuronal culture media provide very different conditions than those observed in the living brain and profoundly impair essential neurophysiological functions. (This thesis)
2. A new neuronal medium (BrainPhys™ basal + serum-free supplements) in which we adjusted the concentrations of neuroactive amino acids, inorganic salts and energetic substrates, supports essential electrophysiological neuronal properties while sustaining survival of human neurons in culture. (This thesis)
3. Long-term culture of human neurons in BrainPhys™ basal+sup medium enhances neuronal synaptic function. It is more likely that this synaptic enhancement is due to activation/strengthening of silent synaptic contacts rather than to formation of new synapses. (This thesis)
4. The inherent variation in basic electrophysiological profiles of human stem cell-derived neurons can be largely explained by two action potential metrics (amplitude and firing rate), which together enable categorization of neurons into five functional types that may represent a neurodevelopmental continuum. (This thesis)
5. “Path-seq profiling” of single neurons enables prediction of functional neuronal states by molecular determinants, independently of time spent in vitro. This opens a new way for isolating highly functional neuron states from heterogeneous cultures using fluorescent markers. (This thesis)
6. To identify accurate neuronal phenotypes between cell lines (e.g., patients vs. healthy subjects), it is essential to compare neurons of equivalent functional (maturational) states. Doing so is likely to improve the rate of translational success of preclinical human stem cell-based research investigations. (This thesis – Valorization addendum)
7. “It’s the individual cell that makes a decision.” (Timm Schroeder)
8. Cells are like animals: their behavior is most accurately expressed when they are studied within their natural habitat.
9. One cannot hypothesize effects “with all other factors remaining constant”, when certain factors were not constant to begin with.
10. The future is ours to manipulate.